ORIGINAL ARTICLE

Emergence of plasmid-mediated quinolone-resistant determinants in *Klebsiella pneumoniae* isolates from Tehran and Qazvin provinces, Iran

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Key words

Klebsiella pneumoniae • Quinolones resistance • *qnr*

Summary

Background. *Plasmid-mediated quinolone resistance is an increasing clinical concern, globally. The major objective of the present study was to identify the qnr-encoding genes among the quinolone non-susceptible K. pneumoniae isolates obtained from two provinces in Iran.*
Methods. *A total of 200 K. pneumoniae isolates were obtained from hospitals of Qazvin and Tehran, Iran. The identification of bacterial isolates was carried out by standard laboratory methods and API 20E strips. Susceptibility to quinolone compounds were examined by standard Kirby-Bauer disk diffusion method according to the CLSI guideline. PCR and sequencing were employed to detect qnrA, qnrB and qnrS-encoding genes.*
Results. *Of 200 K. pneumoniae isolates, 124 (62%) were non-susceptible to quinolone compounds among those 66 (53.2%) and 58 (46.8%) isolates showed high and low-level quinolone resistance rates, respectively. Out of 124 quinolone non-susceptible isolates, qnr-encoding genes were present in 49 (39.5%) isolates with qnrB1 (30.6%) as the most dominant gene followed by qnrB4 (9.7%), and qnrS1 (1.6%) either alone or in combination.*
Conclusions. *This study, for the first time, revealed the high appearance of qnrB1, qnrS1 and qnrB4 genes among the clinical isolates of K. pneumoniae in Iran. Therefore, the application of proper infection control measures and well-established antibiotic administration guideline should be strictly considered within our medical centers.*

Introduction

Klebsiella pneumoniae (K. pneumoniae) is an opportunistic pathogen causing several nosocomial infections such as urinary tract infections, pneumonia, septicemia, and soft tissue infections [1]. This organism is also known as a community-acquired potential pathogen [2]. Health care associated infection caused by this organism has been linked to high mortality and morbidity especially among the patients admitted to intensive care units [3, 4].
Quinolones are a group of synthetic antibacterial agents that are widely used in routine clinical practice [5]. The new quinolones compounds (6-fluoroquinolones) exhibit broad spectrum of antibacterial activity against Gram-negative, mycobacterial pathogens, and anaerobes. Moreover, these agents show a good-to-moderate oral absorption and tissue penetration with favorable pharmacokinetics in humans, creating desirable clinical efficacy in treating many kinds of infections [6, 7]. Quinolones inhibit the function of bacterial DNA gyrase and topoisomerase IV [8]. While the first and second generation fluoroquinolones selectively inhibit the topoisomerase II ligase domain or DNA gyrase activity, the quinolones of third and fourth generations are with more tendency for topoisomerase IV ligase [9]. Excessive and inappropriate administration of antimicrobial agents such as quinolones has increased the emergence of multidrug resistant *K. pneumoniae* isolates which makes the process of antimicrobial therapy to become marginal and problematic [10, 11]. In recent years, several studies have demonstrated that the appearance of quinolone-resistant *K. pneumoniae* is rising at a faster rate, worldwide [12-15]. Infections caused by resistant organisms are often due to extensive cross-resistance with other antimicrobials, including beta-lactams and aminoglycosides [16]. Quinolone resistance in *Enterobacteriaceae* mainly occurs through chromosomal mutations in the genes coding for DNA gyrase and topoisomerase IV, changes in outer membrane and efflux proteins or in their regulatory mechanisms [17]. Findings from recent studies show that plasmid-mediated resistance, associated with the pentapeptide proteins of the *qnr* family, might play a crucial role in quinolone compound resistance [18]. Three major groups of *qnr* determinants, *qnrA*, *qnrB*, and *qnrS*, are increasingly being identified in the clinical isolates of various enterobacterial species, worldwide [19]. It was in 1998 that the first plasmid-mediated quinolone resistance determinant, *qnrA*, was reported in a *Klebsiella pneumoniae* strain from the United States [20]. Since then two *qnr* determinants, *qnrB* and *qnrS* have been discovered in other *Enterobacte-*